

Case reports

Journal of Medical Genetics 1987, **24**, 172-184

Microcephaly, microphthalmos, and retinal folds: report of a family

I D YOUNG*, A R FIELDER†, AND K SIMPSON*

Departments of Child Health and Ophthalmology†, Leicester Royal Infirmary, Leicester LE2 7LX.*

SUMMARY A retarded boy with microcephaly, microphthalmos, and retinal folds is described. His mother and sister showed microphthalmos and the sister was also microcephalic. Another family showing similar findings has been described, indicating that this combination of abnormalities constitutes a discrete entity showing single gene inheritance.

In 1981, Jarmas *et al*¹ described two brothers each of whom had severe microcephaly, microphthalmos, falciform retinal folds, and visual deficit. Their mother was also microcephalic and showed mild mental retardation. We now describe a third patient with similar findings. His mother and sister showed milder manifestations of the same disorder.

Case report

The proband weighed 2.5 kg when born at 34 weeks after an uneventful, drug free pregnancy. Bilateral pedal oedema was present at birth and disappeared by the age of three months. The neonatal period was otherwise uncomplicated and no additional oxygen was given at any time.

At six months he presented with impaired central vision and was noted to have a divergent squint and to be microcephalic (OFC = 36.5 cm), with a closed anterior fontanelle. Examination under general anaesthesia revealed bilaterally reduced horizontal corneal diameters (10.0 mm right and left, normal = 11.64 ± 0.49 mm [$\pm 2SD$]). Both lenses were clear. The right fundus contained a falciform vitreoretinal fold, into which all the retinal vessels were drawn, extending from the optic disc (fig 1). As the fold approached the temporal periphery, vitreous bands branched and were inserted circumferentially an-

terior to the ora serrata. In the left fundus there was temporal dragging of the optic disc with extensive scarring temporally (fig 2), while inferiorly there was a 'crazy paving' pattern suggestive of cracks in the retinal pigment epithelium. Vitreous strands were present temporally. Mydriatic refraction at a later date revealed hypermetropia with astigmatism more pronounced on the right (+5.0 D.sphere with +2.0 D.cylinder at 90°) than the left (+1.0 D.sphere with +2.0 D.cylinder at 90°).

The patient was reassessed at two years five

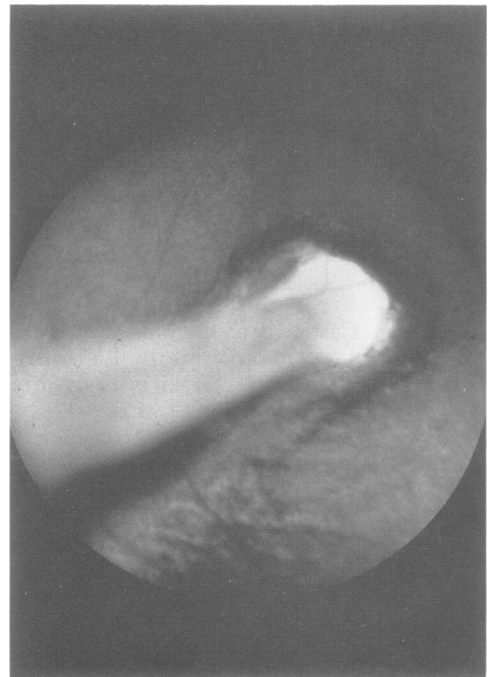


FIG 1 The proband's right fundus at six months of age.

Received for publication 30 August 1985.

Revised version accepted for publication 3 October 1985.

months, when he was again noted to have impaired central vision but good peripheral fields. Mild cognitive delay was apparent with a mental age of 19 months on the Bayley mental scales. On examination his head circumference was 42.5 cm (4 cm below the 3rd centile) with height and weight falling

on the 10th centile. He had a narrow, sloping forehead (fig 3) and bilateral fifth finger clinodactyly, with no other dysmorphic features. Apart from the ocular findings, neurological examination was normal.

Investigations giving normal results included congenital infection screen, banded karyotype, blood and urine amino acids, and audiology. There was no evidence of craniostenosis on skull x ray.

Family history

The proband was the second child of unrelated parents. At the age of six years his older sister was noted to have bilateral microphthalmia (corneal diameters 9.5 and 10.0 mm) with normal fundi, strabismus, and microcephaly (OFC = 46.7 cm). Her cognitive abilities were below average but she was able to attend normal school. His younger brother was examined and found to be entirely normal.

The father and paternal grandmother were of normal intelligence with normal eyes and head size, as was the maternal grandmother. The proband's mother was of normal intelligence with a head circumference of 55.0 cm. Her fundi were normal but both eyes were small with corneal diameters of 10.5 mm. Her Guthrie test and urinary amino acid screen were normal. All fundal examinations were performed after pupil dilatation.

Discussion

Retinal folds have recently been the subject of a comprehensive review.² Aetiologically they may result from either a malformation, often in association with strands of primary vitreous as in the boy

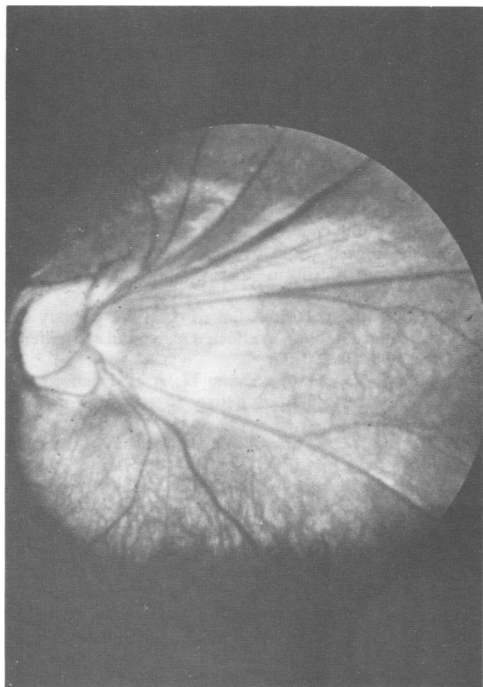


FIG 2 The proband's left fundus at six months of age.



FIG 3 The proband with his older sister.

now described, or from insult occurring after organogenesis, such as infection or retinopathy of prematurity (ROP). Although born prematurely, our patient had no neonatal problems and he did not require oxygen therapy. ROP has been reported in similar circumstances but the ocular signs are different. The boy we describe is hypermetropic whereas in cicatricial ROP, myopia is the rule and extensive vitreous bands are not seen.

From the genetic viewpoint retinal folds are found in several entities. In isolation they may show autosomal dominant, autosomal recessive, or sex linked recessive inheritance.² In this latter form minor ocular abnormalities may be detected in carrier females.³ They may also be a manifestation of autosomal dominant familial exudative vitreoretinopathy⁴ but insert equatorially in this condition, whereas in the present case the vitreous strands extend further forwards to the ora serrata. Furthermore, no retinal changes have been detected in other family members.

Pleiotropic autosomal recessive syndromes which may feature retinal folds include the Seckel-like syndrome described by Bixler and Antley⁵ and the combination of hydrocephalus with microphthalmos documented by Warburg.⁶ Retinal folds have also been observed in one of four patients who had a sex linked recessive disorder characterised by microphthalmos, corneal clouding, cataracts, microcephaly, hypospadias, and cryptorchidism,⁷ and in a blind retarded boy who was found to have an interstitial deletion of the long arm of chromosome 13.⁸

The combination of microcephaly, microphthalmos, and retinal folds has been described in a male offspring of first cousin parents,⁹ to a variable degree in four persons from two sibships in a large inbred family,¹⁰ and in the aforementioned brothers reported by Jarmas *et al.*¹ One of these brothers also had pedal oedema and both showed mildly anteverted nares, these features also being present in our

own patient, in whom the pedal oedema resolved slowly over the first three months of life. In the family of Jarmas *et al.*¹ the boys' mother showed microcephaly and microphthalmos. Taken in conjunction with the findings in our patient's mother and sister, this would suggest that there is an inherited form of microcephaly, microphthalmos, and retinal folds in which males show the full stigmata with females being more mildly affected. Inheritance could be sex linked dominant or sex influenced autosomal dominant.

References

- Jarmas AL, Weaver DD, Ellis FD, Davis A. Microcephaly, microphthalmia, falciform retinal folds and blindness. *Am J Dis Child* 1981;135:930-3.
- Warburg M. Retinal malformations. Aetiological heterogeneity and morphological similarity in congenital retinal non-attachment and falciform folds. *Trans Ophthalm Soc UK* 1979;99:272-83.
- Godel V, Goodman RM. X-linked recessive primary retinal dysplasia: clinical findings in affected males and carrier females. *Clin Genet* 1981;20:260-6.
- Nishimura M, Yamana T, Sugino M, *et al.* Falciform retinal fold as sign of familial exudative vitreoretinopathy. *Jpn J Ophthalmol* 1983;27:40-53.
- Bixler D, Antley RM. Microcephalic dwarfism in sisters. *Birth Defects* 1974;X(7):161-5.
- Warburg M. Hydrocephaly, congenital retinal non-attachment and congenital falciform fold. *Am J Ophthalmol* 1978;85:88-94.
- Duker JS, Weiss JS, Siber M, Bieber FR, Albert DM. Ocular findings in a new heritable syndrome of brain, eye and urogenital abnormalities. *Am J Ophthalmol* 1985;99:51-5.
- Judberg RC, Mowrey PN. Interstitial del (13q) associated with blindness and mental retardation. *Am J Med Genet* 1984;17:609-13.
- Gartner S. Congenital retinal folds and microcephaly. *Arch Ophthalmol* 1941;25:93-100.
- Masuda Y. Two cases of ablatio falciformis congenita and two other cases of ocular congenital anomalies, which appeared in a pedigree with consanguineous marriages. *Jpn J Clin Ophthalmol* 1962;16:325-31.

Correspondence and requests for reprints to Dr I D Young, Department of Child Health, Clinical Sciences Building, Leicester Royal Infirmary, PO Box 65, Leicester LE2 7LX.

A de novo 3p;8p unbalanced translocation resulting in partial dup(3p) and partial del(8p)

P R SCARBROUGH*, A J CARROLL*, W H FINLEY*†, AND D R BRIDGES*

*Laboratory of Medical Genetics, and †Department of Pediatrics, University of Alabama at Birmingham, Birmingham, Alabama, USA.

SUMMARY We present the first case of a de novo translocation resulting in dup(3p). Giemsa banding studies tentatively identified the

source of the extra genetic material as 3p. Clinical findings were compatible with those previously reported in dup(3p) patients, further defining this cytogenetic anomaly as a distinct, clinically identifiable syndrome.